



SEQUENCE LISTING

<110> BAKER, Matthew
WATKINS, John

<120> MODIFIED HIRUDIN PROTEINS AND T-CELL
EPITOPES IN HIRUDIN

<130> MER-142

<140> US 10/560,918

<141> 2005-12-16

<150> PCT/EP2004/006943

<151> 2004-06-25

<150> EP 03014332.5

<151> 2003-06-26

<160> 108

<170> FastSEQ for Windows Version 4.0

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<212> PRT

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<222> 13, 15, 21, 29

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X=A, G, H, K, N, P, Q, R, V;

X=A, D, E, G, H, K, N, Q, R, S, T, I;

<221> VARIANT

<222> 30, 40, 47, 48

<223> X=A, D, E, G, H, K, N, P, Q, R, S, T, L;

X=A, T, V;

X=T, K;

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<221> VARIANT

<222> 53, 56

<223> X=E, N, R, D;
X=H, F

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			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Xaa	Thr	Gly	Glu	Gly	Thr	Pro	Xaa	Xaa
		35					40					45			
Glu	Ser	His	Asn	Xaa	Gly	Asp	Xaa	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
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<400> 3

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
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Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
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Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ala	Ala	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
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Gln															
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Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Arg	His	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
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Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Glu	Lys	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Ala	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
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Gln															
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Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Glu	Lys	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Thr	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
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 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Glu Lys Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Glu Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
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<210> 9
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<400> 9
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 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Glu Lys Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asn Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
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 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Arg Lys Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Ala Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln

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<400> 11
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
1 5 10 15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Arg Lys Gly Ser
20 25 30
Asp Gly Glu Lys Asn Gln Cys Thr Thr Gly Glu Gly Thr Pro Lys Pro
35 40 45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
50 55 60
Gln
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<400> 12
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
1 5 10 15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Arg Lys Gly Ser
20 25 30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
35 40 45
Glu Ser His Asn Glu Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
50 55 60
Gln
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<400> 13
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
1 5 10 15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Arg Lys Gly Ser
20 25 30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
35 40 45

Glu Ser His Asn Asn Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
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 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Arg Arg Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Thr Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
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 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ala Lys Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
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<210> 16
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<220>
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<400> 16
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 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ala Gln Gly Ser

		20					25					30					
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro		
		35					40					45					
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu		
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Gln																	
65																	

<210> 17
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Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys		
1				5					10					15			
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ala	Arg	Gly	Ser		
			20					25					30				
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro		
		35				40					45						
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu		
		50				55					60						
Gln																	
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<210> 18
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1				5					10					15			
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ala	Thr	Gly	Ser		
			20					25					30				
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro		
		35				40					45						
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu		
		50				55					60						
Gln																	
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<210> 19
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<220>
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<400> 19

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Asp	Ala	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
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<220>
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Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Asp	Gln	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
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Gln															
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Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Asp	Arg	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
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Gln															
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<210> 22
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<220>

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<400> 22

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Glu	Lys	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
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Gln															
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<210> 23

<211> 65

<212> PRT

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<220>

<223> modified hirudin

<400> 23

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Glu	Gln	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
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Gln															
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<210> 24

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<400> 24

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Glu	Arg	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
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<210> 25

<211> 65

<212> PRT

<213> Artificial Sequence

<220>

<223> modified hirudin

<400> 25

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Glu	Thr	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
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<210> 26

<211> 65

<212> PRT

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<220>

<223> modified hirudin

<400> 26

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Arg	Lys	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
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<210> 27

<211> 65

<212> PRT

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<220>

<223> modified hirudin

<400> 27

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Arg	Gln	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
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<400> 28
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Arg Arg Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
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<210> 29
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<220>
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<400> 29
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Arg Thr Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
 65

<210> 30
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<220>
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<400> 30
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 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ser Ala Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln

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<400> 31
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
1 5 10 15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ser Lys Gly Ser
20 25 30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
35 40 45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
50 55 60
Gln
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<210> 32
<211> 65
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<213> Artificial Sequence

<220>
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<400> 32
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
1 5 10 15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ser Gln Gly Ser
20 25 30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
35 40 45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
50 55 60
Gln
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<210> 33
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<220>
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<400> 33
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
1 5 10 15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ser Arg Gly Ser
20 25 30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
35 40 45

Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
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<400> 34
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ser Thr Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
 65

<210> 35
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<400> 35
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
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 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Thr Ala Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
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<210> 36
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<220>
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<400> 36
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Thr Lys Gly Ser

		20						25					30				
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro		
		35					40					45					
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu		
		50				55					60						
Gln																	
65																	

<210> 37
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<220>
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Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys		
1				5					10					15			
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Thr	Gln	Gly	Ser		
			20					25					30				
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro		
		35				40					45						
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu		
		50				55					60						
Gln																	
65																	

<210> 38
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys		
1				5					10					15			
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Thr	Arg	Gly	Ser		
			20					25					30				
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro		
		35				40					45						
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu		
		50				55					60						
Gln																	
65																	

<210> 39
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

<400> 39

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Thr	Thr	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 40
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Thr	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 41
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Ala	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 42
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>

<223> modified hirudin

<400> 42

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	His	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser
			20					25				30			
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 43

<211> 65

<212> PRT

<213> Artificial Sequence

<220>

<223> modified hirudin

<400> 43

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Gln	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser
			20					25				30			
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 44

<211> 65

<212> PRT

<213> Artificial Sequence

<220>

<223> modified hirudin

<400> 44

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Thr	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser
			20					25				30			
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 45

<211> 65

<212> PRT

<213> Artificial Sequence

<220>

<223> modified hirudin

<400> 45

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Ala	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 46

<211> 65

<212> PRT

<213> Artificial Sequence

<220>

<223> modified hirudin

<400> 46

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Gly	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 47

<211> 65

<212> PRT

<213> Artificial Sequence

<220>

<223> modified hirudin

<400> 47

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	His	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 48
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

<400> 48
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1 5 10 15
 Glu Gly Ser Val Lys Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
 65

<210> 49
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

<400> 49
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1 5 10 15
 Glu Gly Ser Val Asn Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
 65

<210> 50
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

<400> 50
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1 5 10 15
 Glu Gly Ser Val Pro Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln

65

<210> 51
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 51
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
1 5 10 15
Glu Gly Ser Val Gln Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
20 25 30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
35 40 45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
50 55 60
Gln
65

<210> 52
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 52
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
1 5 10 15
Glu Gly Ser Val Arg Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
20 25 30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
35 40 45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
50 55 60
Gln
65

<210> 53
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 53
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
1 5 10 15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ala Leu Gly Ser
20 25 30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
35 40 45

Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
 65

<210> 54
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

<400> 54
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Asp Leu Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
 65

<210> 55
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

<400> 55
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Glu Leu Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
 65

<210> 56
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

<400> 56
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Gly Leu Gly Ser

		20						25					30				
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro		
		35					40					45					
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu		
		50				55					60						
Gln																	
65																	

<210> 57
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys		
1				5					10					15			
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	His	Leu	Gly	Ser		
			20					25					30				
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro		
		35				40					45						
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu		
		50				55					60						
Gln																	
65																	

<210> 58
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys		
1				5					10					15			
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Lys	Leu	Gly	Ser		
			20					25					30				
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro		
		35				40					45						
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu		
		50				55					60						
Gln																	
65																	

<210> 59
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

<400> 59

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Asn	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 60
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Gln	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 61
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Arg	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 62
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>

<223> modified hirudin

<400> 62

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ser	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 63

<211> 65

<212> PRT

<213> Artificial Sequence

<220>

<223> modified hirudin

<400> 63

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Thr	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 64

<211> 65

<212> PRT

<213> Artificial Sequence

<220>

<223> modified hirudin

<400> 64

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Ala	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 65

<211> 65

<212> PRT

<213> Artificial Sequence

<220>

<223> modified hirudin

<400> 65

```
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1           5           10           15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Asp Gly Ser
          20           25           30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
          35           40           45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50           55           60
Gln
65
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<210> 66

<211> 65

<212> PRT

<213> Artificial Sequence

<220>

<223> modified hirudin

<400> 66

```
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1           5           10           15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Glu Gly Ser
          20           25           30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
          35           40           45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50           55           60
Gln
65
```

<210> 67

<211> 65

<212> PRT

<213> Artificial Sequence

<220>

<223> modified hirudin

<400> 67

```
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1           5           10           15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Gly Gly Ser
          20           25           30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
          35           40           45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50           55           60
Gln
65
```


<210> 68
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

<400> 68
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile His Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
 65

<210> 69
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

<400> 69
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Lys Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
 65

<210> 70
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

<400> 70
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Asn Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln

65

<210> 71
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 71
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
1 5 10 15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Pro Gly Ser
20 25 30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
35 40 45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
50 55 60
Gln
65

<210> 72
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 72
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
1 5 10 15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Gln Gly Ser
20 25 30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
35 40 45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
50 55 60
Gln
65

<210> 73
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 73
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
1 5 10 15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Arg Gly Ser
20 25 30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
35 40 45

Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
 65

<210> 74
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

<400> 74
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Ser Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
 65

<210> 75
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

<400> 75
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Thr Gly Ser
 20 25 30
 Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 35 40 45
 Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
 50 55 60
 Gln
 65

<210> 76
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

<400> 76
 Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1 5 10 15
 Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser

		20						25					30				
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Ala	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro		
		35					40					45					
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu		
		50				55					60						
Gln																	
65																	

<210> 77
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys		
1				5					10					15			
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser		
			20					25					30				
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Thr	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro		
		35				40					45						
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu		
		50				55					60						
Gln																	
65																	

<210> 78
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys		
1				5					10					15			
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser		
			20					25					30				
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Thr	Pro		
		35				40					45						
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu		
		50				55					60						
Gln																	
65																	

<210> 79
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

<400> 79

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Ala
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 80
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Thr
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 81
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> modified hirudin

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Glu	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 82
 <211> 65
 <212> PRT
 <213> Artificial Sequence

<220>

<223> modified hirudin

<400> 82

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asn	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 83

<211> 65

<212> PRT

<213> Artificial Sequence

<220>

<223> modified hirudin

<400> 83

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Arg	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 84

<211> 65

<212> PRT

<213> Artificial Sequence

<220>

<223> modified hirudin

<400> 84

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys
1				5					10					15	
Glu	Gly	Ser	Val	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser
			20					25					30		
Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
		35					40					45			
Glu	Ser	His	Asn	Asp	Gly	Asp	His	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Leu
	50					55					60				
Gln															
65															

<210> 85

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> secretion signal

<400> 85

Met	Phe	Ser	Leu	Lys	Leu	Phe	Val	Val	Phe	Leu	Ala	Val	Cys	Ile	Cys
1				5					10					15	
Val	Ser	Gln	Ala												
			20												

<210> 86

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> secretion signal

<400> 86

Met	Val	Ser	Leu	Lys	Leu	Phe	Val	Val	Phe	Leu	Ala	Val	Cys	Ile	Cys
1				5					10					15	
Val	Ser	Gln	Ala												
			20												

<210> 87

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 87

Val	Val	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu
1				5					10					15

<210> 88

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 88

Leu	Thr	Tyr	Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu
1				5					10					15

<210> 89

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 89

Thr	Asp	Cys	Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys	Glu	Gly
1				5					10					15

<210> 90

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 90

Thr	Glu	Ser	Gly	Gln	Asn	Leu	Cys	Leu	Cys	Glu	Gly	Ser	Asn	Val
1				5				10					15	

<210> 91

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 91

Gly	Gln	Asn	Leu	Cys	Leu	Cys	Glu	Gly	Ser	Asn	Val	Cys	Gly	Gln
1				5				10					15	

<210> 92

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 92

Leu	Cys	Leu	Cys	Glu	Gly	Ser	Asn	Val	Cys	Gly	Gln	Gly	Asn	Lys
1				5				10					15	

<210> 93

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 93

Cys	Glu	Gly	Ser	Asn	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu
1				5				10					15	

<210> 94

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 94

Ser	Asn	Val	Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser	Asp
1				5				10					15	

<210> 95

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 95

Cys	Gly	Gln	Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser	Asp	Gly	Glu	Lys
1				5				10					15	

<210> 96

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 96

Gly	Asn	Lys	Cys	Ile	Leu	Gly	Ser	Asp	Gly	Glu	Lys	Asn	Gln	Cys
1				5					10					15

<210> 97

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 97

Cys	Ile	Leu	Gly	Ser	Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly
1				5					10					15

<210> 98

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 98

Gly	Ser	Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr
1				5					10					15

<210> 99

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 99

Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro
1				5					10					15

<210> 100

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 100

Asn	Gln	Cys	Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro	Glu	Ser	His
1				5					10					15

<210> 101

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 101

Val	Thr	Gly	Glu	Gly	Thr	Pro	Lys	Pro	Glu	Ser	His	Asn	Asp	Gly
1				5					10					15

<210> 102

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 102

Glu	Gly	Thr	Pro	Lys	Pro	Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu
1				5					10					15

<210> 103

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 103

Pro	Lys	Pro	Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro
1				5					10					15

<210> 104

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 104

Glu	Ser	His	Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr
1				5					10					15

<210> 105

<211> 15

<212> PRT

<213> hirudo medicinalis

<400> 105

Asn	Asp	Gly	Asp	Phe	Glu	Glu	Ile	Pro	Glu	Glu	Tyr	Tyr	Leu	Gln
1				5					10					15

<210> 106

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> modified hirudin sequence

<400> 106

Cys	Ala	Ala	Gly	Ser	Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly
1				5					10					15

<210> 107

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> modified hirudin sequence

<400> 107

Cys	Glu	Lys	Gly	Ser	Asp	Gly	Glu	Lys	Asn	Gln	Cys	Val	Thr	Gly
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

